IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter Defendants.	[redacted]

NIPPON SHINYAKU CO., LTD. AND NS PHARMA, INC.'S MOTION TO EXCLUDE OPINIONS OF DR. STEVEN DOWDY, PH. D.

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I. INTRODUCTION

When NS moved *in limine* to bar Sarepta's reliance on post-priority date art to support written description and enablement, Sarepta avoided a "blanket exclusion" by arguing that "the evidence we're relying on is for the purpose of illuminating the state of the art as of the priority date." *See, e.g.*, D.I. 570, Hr'g Tr. (May 6, 2024) at 11:3-6, 16-18. But Dr. Dowdy's supplemental opinions go far beyond Sarepta's representation. Dr. Dowdy casts the discovery of new species ***years after*** the priority date as supposedly "confirming" the alleged earlier disclosure of a "structure-function" correlation. But Dr. Dowdy agrees that "data that was not available in June 2005 [*i.e.*, the '851 Patent's priority date] ***would not reflect the understanding of a POSA at that time***."[1] Ex. D.I. 604-10, Dowdy Suppl. Dep. at 364:5-9. The Court should therefore exclude Dr. Dowdy's opinions relying on later-discovered species as supposedly "confirming" a structure-function correlation, as they are unreliable and unhelpful to the trier of fact.

II. LEGAL STANDARD

"[P]ost-priority date evidence proffered to illuminate the post-priority-date state of the art [] is improper." *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1373-75 (Fed. Cir. 2017). This is because "the hallmark of written description is disclosure," and "the four corners of the specification" must demonstrate possession of the claimed invention. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). Likewise, "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1159 (Fed. Cir. 2019).

In *Juno*, the Federal Circuit considered the inventors' "testimony about post-priority date developments"—that they made additional species after-the-fact. *Juno Therapeutics, Inc. v. Kite*

[1] Emphasis is added throughout unless noted otherwise.

Pharma, Inc., 10 F.4th 1330, 1341 (Fed. Cir. 2021). The Federal Circuit held that later discovery of those species was "irrelevant" to showing possession of the claimed invention as of its priority date. *Id.* Similarly, in *Biogen*, the Federal Circuit recognized "[t]hat Biogen later established the therapeutic efficacy of DMF480 is of no import." *Biogen Int'l GMBH v. Mylan Pharms. Inc*., 18 F.4th 1333, 1343-44 (Fed. Cir. 2021). Even Sarepta conceded that "***certain types*** of patentee post-priority evidence were found to be irrelevant to written description," namely evidence showing "***new discoveries and developments***." D.I. 536-15 (Ex. 14A.2) at 2, n.2 (emphasis in original).

III. ARGUMENT

The '851 Patent claims a genus of ASOs that induce exon 53 skipping and meet the recited structural criteria. Sarepta contends there are only 168 candidate species within the genus (based on the 168 distinct target regions in the exon 53 pre-mRNA). D.I. 604-7, Dowdy Suppl. Reb. ¶16, Tbl. 1. Dr. Dowdy concedes that testing is required to determine whether an ASO meeting the structural criteria (a candidate) will meet the claim's functional requirement. D.I. 604-10, Dowdy Suppl. Dep. at 258:23-259:8; D.I. 604-9, Dowdy Dep. at 44:11-15. In other words, a candidate ASO cannot be definitively classified as a species unless it is tested and shown to induce exon 53 skipping. D.I. 604-7, Dowdy Suppl. Reb. ¶18. As Dr. Dowdy confirmed, even under the Court's new construction there is at most only "one representative species" disclosed in the specification and tested by Dr. Wilton.[2] D.I. 604-10, Dowdy Suppl. Dep. at 287:20-288:8, 316:20-24. That sole ASO only "demonstrated weak skipping." *Id.* at 316:25-317:4.

To support an alleged structure-function correlation in the absence of evidence in the specification, Dr. Dowdy's supplemental report relies on post-priority date discoveries of new

[2] Defendants accept Dr. Dowdy's position that this species was representative for purposes of this motion only. The claims of the '851 Patent require the ASO to be a "morpholino," but the '851 Patent reports exon skipping data for a different chemistry. D.I. 604-10, Dowdy Suppl. Dep. at 289:16-20.

morpholino ASOs within the claimed genus. *See, e.g.*, Ex. D.I. 604-7, Dowdy Suppl. Reb. ¶13 ("[N]umerous researchers . . . have repeatedly confirmed this relationship ***since June 2005***."); ¶90 ("***Subsequent studies*** from multiple research groups confirm this expectation" that most claimed ASOs "would induce exon 53 skipping"); ¶120 ("[N]umerous studies from multiple independent research groups repeatedly confirmed Dr. Wilton's exon 53 hot spot."); *see also* D.I. 427-2, Dowdy Reb. ¶92 (summarizing post-priority date testing as "*confirm[ing]* that the claimed structural features . . . confer the claimed function").

Likewise, when asked at his supplemental deposition about disclosures providing "support for an area of activity or amenable region . . . ***within the specification***," Dr. Dowdy testified, unprompted: "And I would add subsequently, every oligo that fulfills Claim 1 induces exon skipping." D.I. 604-10, Dowdy Suppl. Dep. at 263:8-19. Similarly, when asked to confirm that none of the exon 53 ASOs disclosed in the specification have been tested in clinical trials, Dr. Dowdy noted that later, there were "two [species] that have gone into clinical trials." *Id.* at 316:2-19; *see also id.* 331:18-332:13 (stating that the genus "includes two FDA-approved PMO oligonucleotides to exon 53 that are clinically validated").

Assuming he will testify consistently in front of the jury, Dr. Dowdy will rely on ***later-discovered*** species that have (1) different base sequences; (2) a different backbone chemistry (morpholino); and (3) different levels of functional activity than the exon 53 ASOs disclosed in the specification to argue for a structure-function correlation between structural elements required by the claims and the claimed function of exon 53 skipping. D.I. 427-2, Dowdy Reb. ¶92, Fig. 13. But, as noted above in Section II, *supra*, data from after-the-fact functional testing cannot "confirm" and is not relevant to the understanding of a POSA as of the '851 Patent's June 28, 2005

priority date.[3] Dr. Dowdy's anticipated testimony on species that were only discovered to be species (rather than candidates) ***after*** the priority date cannot illuminate the state of the art as of the priority date and will not help the jury. Rather, it serves only to confuse jurors and improperly suggest that later discoveries of previously-untested species may compensate for the '851 Patent's deficient disclosure. It should be excluded.

IV. CONCLUSION

The Court should exclude Dr. Dowdy's reliance on post-priority date testing of ASOs to support his alleged "structure-function" correlation as unreliable and unhelpful to the trier of fact. *See* Fed. R. Evid. 702.

[3] Even Dr. Dowdy agrees; he disputed the relevance of certain post-priority date testing relied upon by NS's expert, Dr. Michelle Hastings, arguing that it "was not available in June 2005, and thus could not reflect the understanding of a POSA as of that time." Ex. A, Dowdy Suppl. Reb. ¶119. Dr. Dowdy confirmed this view at his supplemental deposition:

> Q. So you would agree in your view, data that was not available in June 2005 would not reflect the understanding of a POSA at that time.
>
> A. **Correct.** All of that is after the fact in terms of ascertaining the value of that.

D.I. 604-10, Dowdy Suppl. Dep. at 364:5-9

October 2, 2024

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned certifies that on October 2, 2024, a copy of the foregoing, NIPPON SHINYAKU CO., LTD. AND NS PHARMA, INC.'S MOTION TO EXCLUDE OPINIONS OF DR. STEVEN DOWDY, PH. D., which was filed under seal, was served via electronic mail on the following counsel of record:

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